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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/638,358	08/15/2000	Joseph D. Mosca	640100-383	1532

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Raymond J Lillie Esq
Carella Byrne Bain Gilfillan Cecchi
Stewart & Olstein
Six Becker Farm Road
Roseland, NJ 07068

EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/05/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/638,358	Mosca
Examiner	**Art Unit**
Anne Marie Wehbé	1632

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Aug 13, 2002*.

2a) [X] This action is **FINAL**. 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-15* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-15* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other: _____

DETAILED ACTION

Applicant's request for reconsideration received on 8/13/02 has been entered. Claims 1-15 are pending and active in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in previous office actions.

Claim Rejections - 35 USC § 112

The rejection of claims 1-15 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the office has not provided any evidence other than speculation that the disclosed compositions could not be used as vaccines. In response, it is noted that the previous office action analyzed the specification in direct accordance to the factors outlined in *In re Wands*, namely 1) the nature of the invention, 2) the state of the prior art, 3) the predictability of the art, 4) the amount of direction or guidance present, and 5) the presence or absence of working examples, and presented detailed scientific reasons supported by publications from the

prior art for the finding of a lack of enablement for the instant claims. Please note that case law including the Marzocchi decision sanctions both the use of sound scientific reasoning and printed publications to support a holding of non-enablement (see *In re Marzocchi* 169 USPQ 367, and *Ex parte Sudilovsky* 21 USPQ2d 1702). Further, the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh,* 17 USPQ2d 1714 (BPAI 1991). 35 U.S.C. 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). Case law also states that ".. the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not to find out how to use it for themselves." *In re Gardner* 166 USPQ 138 (CCPA) 1970. Based on a proper analysis of the specification according to *In re Wands* as discussed above and presented in detail in the previous office action, the office finds that the instant specification does not provide a disclosure of the instant invention which "reasonably correlates" with the scope of the claims as written. The applicant has not presented any specific arguments or evidence regarding the issues raised in the previous office action.

The applicant also states that not all embodiments encompassed within a claim must be operable for the claims to be valid, citing *Ex Parte Mark*. The applicant's claims as written specifically recite a "vaccine". The word "vaccine" is a well understood medical term, generally defined as a preparation used to protect against disease, primarily pathogenic disease. Thus,

recitation of the term "vaccine" defines the applicant's claimed invention as a composition which is capable of preventing disease. The previous office action indicated that while the specification is enabling for **compositions** comprising mesenchymal stem cells or cells of the adipocyte lineage which have been transfected with a co-stimulatory molecule and have been further modified to present an antigen epitope on MHC class II, it does not reasonably provide enablement for the use of said compositions as vaccines to prevent any and all diseases. Were applicants to amend the claims to recite a "composition" rather than a "vaccine", then applicants citation of *Ex Parte Marks* would be relevant. However, since the specification does not enable any **vaccine** according to the instant claims, the claims as written do not appear to encompass any operable embodiment. The applicant is also reminded that case law states that, " if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid". See, e.g., *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971).

The rejection of claims 1-15 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements is maintained. Applicant's request for reconsideration fails to address this issue. Therefore, the rejection of record stands.

Claim Rejections - 35 USC § 103

The rejection of claims 1-15 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,962,320 (10/5/99), hereafter referred to as Robinson et al., in view of U.S. Patent No. 5,591,625 (1/7/97), hereafter referred to as Gerson et al. is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that Robinson et al. does not teach or suggest modifying a mesenchymal stem cell or a cell of the adipocyte lineage to express at least one co-stimulatory molecule and to have at least one exogenous antigen fragment bound to a surface molecule. The applicant also argues that Gerson does not teach mesenchymal stem cells that express at least one co-stimulatory molecule and that have at least one exogenous antigen fragment bound to a surface molecule. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The previous office action stated that Robinson et al. teaches methods of making engineered antigen presenting cells by transfecting cells that are not professional antigen presenting cells with a vector encoding a co-stimulatory molecule such as B7-1 or B7-2 (Robinson et al., columns 21-24, claims 1-26). Robinson et al. further teaches the use of non-professional antigen presenting cells transfected with a nucleic acid

encoding a co-stimulatory molecule and further transfected with a nucleic acid encoding an antigen and an MHC class II molecule for the stimulation of immune responses both *in vitro* and *in vivo* (Robinson et al., columns 7-9). Robinson et al. also teaches that the engineered APCs can be pulsed with exogenous antigen in order to stimulate T cells (Robinson et al., columns 7-8). Finally, Robinson et al. teaches that the engineered APCs can further be modified to express interferon-gamma (Robinson et al., columns 7-9). Gerson et al. was supplied to supplement Robinson et al. by teaching purified human mesenchymal stem cells useful as host cells for the expression of exogenous gene products (Gerson et al., column 1, and column 18, claim 1). Gerson et al. further teaches that the mesenchymal stem cells can be transduced or transfected with a therapeutic gene and administered to a host for treatment of disease (Gerson et al., columns 1-2). Motivation to combine the references was provided by 1) the teachings of Gerson et al that the advantages of transduced mesenchymal stem cells over other type of cells include the ability to express newly introduced genes in the stem cells and their progeny in a less restrictive fashion than other cells, thereby expanding the potential application in treating medical disease (Gerson et al., column 3, lines 12-24), and 2) the teachings of Robinson et al. that any primary non-professional antigen presenting cells can be engineered to induce immune responses.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge

generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). The applicant is further reminded that the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). For the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. *In re Nilssen*, 7 USPQ2d 1500 (Fed. Cir. 1988). In this case, the motivation to combine the references is found in the teachings of both Gerson and Robinson as stated above. As clearly stated in the previous office action, based on the motivation provided by Gerson to use transduced human mesenchymal stem cells for in vivo therapy, and the teachings of Robinson et al. that any primary non-professional antigen presenting cells can be engineered to induce immune responses, it would have been *prima facie* obvious to the skilled artisan to use human mesenchymal stem cells as the primary non-professional antigen presenting cell in the methods of making engineered APCs taught by Robinson et al. Further, in view of the teachings of Gerson et al. regarding the isolation, culturing, and genetic manipulation of mesenchymal stem cells, and the high level of skill in molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in transfecting a mesenchymal stem cell with a vector encoding B7-1 or B7-2, and further modifying the cell to present an antigen bound to MHC class II.

In addition, the applicant is reminded that the species of MHC class II molecule was elected by applicants in paper no. 6; and that for the purposes of prior art, the intended use of the cells as a "vaccine" is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. *In re Casey*, 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER